

Amendments to the Specification:

Please amend the specification as follows:

Please replace the paragraph on page 73, beginning at line 7, with the following rewritten paragraph:

On day two, the transfection reaction was performed. For each vector to be tested, 20 μ l of Lipofectin LIPOFECTIN[®] reagent (Life Technologies Inc., Grand Island, NY) was added to 180 μ l of Optimem OPTIMEM[®] media (Life Technologies Inc., Grand Island, NY), and allowed to incubate at room temperature for 45 minutes. For each" vector to be tested, 2 μ g of vector was mixed into 200 μ g of Optimem OPTIMEM[®] media at 40 minutes. At 45 minutes, minutes, the vector and Lipofectin LIPOFECTIN[®] reagent solutions were ~~mixed~~ mixed together and ,allowed to sit at room temperature for an additional 10 minutes. During this final incubation, the plated host cells were removed from the incubator and washed twice with Optimem OPTIMEM[®] media. At 10 minutes, 1.6 ml of Optimem OPTIMEM[®] media was added to the Lipofectin LIPOFECTIN[®] reagent / vector mix, and 1 ml of the resultant mix was added to each of two cell wells. The host cells were returned to the incubator and allowed to sit undisturbed for 5 hours, at which point the Lipofectin LIPOFECTIN[®] reagent / ~~vector~~ vector mix was removed and replaced by standard cell maintenance media.

Please replace the paragraph on page 48, beginning at line 15, with the following rewritten paragraph:

Certain facilitators of nucleic acid uptake and/or expression ("transfection facilitating agents") can also be included in the compositions, for example, facilitators such as bupivacaine, cardiotoxin and sucrose, and transfection facilitating vehicles such as liposomal or lipid preparations that are routinely used to deliver nucleic acid molecules. Anionic and neutral liposomes are widely available and well known for delivering nucleic acid molecules (see, e.g., Liposomes: A Practical Approach, (1990) RPC New Ed., IRL Press). Cationic lipid preparations are also well known vehicles for use in delivery of nucleic acid molecules. Suitable lipid preparations include DOTMA (N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride), available under the tradename Lipofectin LIPOFECTIN[®],

and DOTAP (1,2-bis(oleyloxy)-3-(trimethylammonio)propane), see, e.g., Felgner et al. (1987) Proc. Natl. Acad. Sci. USA 84:7413-7416; Malone et al. (1989) Proc. Natl. Acad. Sci. USA 86:6077-6081; U.S. Pat. Nos. 5,283,185 and 5,527,928, and International Publication Nos WO 90/11092, WO 91/15501 and WO 95/26356. These cationic lipids may preferably be used in association with a neutral lipid, for example DOPE (dioleyl, phosphatidylethanolamine). Still further transfection-facilitating compositions that can be added to the above lipid or liposome preparations include spermine derivatives (see, e.g., International Publication No. WO 93/18759) and membrane-permeabilizing compounds such as GALA, Gramicidine S and cationic bile salts (see, e.g., International Publication No. WO 93/19768).

Please replace the paragraph on page 75, beginning on line 10, with the following rewritten paragraph:

SCC15 or B16 host cells were transfected as described in Example 9. Eighteen hours post transfection, plates were placed on ice for 15 minutes. Each well was then washed with 2 ml of PBS (Biowhittaker, Walkerville, Md.). Cells were fixed with 0.05% gluteraldehyde (Polysciences Inc, Warrington, Pa.) diluted in PBS and incubated for 30 minutes at room temperature. All subsequent incubations lasted 1 hour at room temperature and washes between each incubation were as stated above. The plates were blocked with 2 ml of 5% dry milk (Bio Rad Laboratories, Melville, N.Y.) in PBS. Incubations with 1 ml of a 1:1000 dilution of anti-gD monoclonal (ABI, Columbia, Md.) in 2% dry milk/PBS 0.05% Tween TWEEN[®]-20 polysorbate surfactant (Sigma, St. Louis, Mo.) and 1 ml of a 1:2500 dilution of goat anti-mouse HRP (KPL, Gaithersburg, Md.) in PBS/0.1% Tween TWEEN[®]-20 polysorbate surfactant followed. Color was developed using 1 ml of TMB microwell substrate (BioFX, Owings Mills, Md.). The reactions were stopped with 1 M H₂SO₄, the liquid was transferred to plastic cuvettes and the optical density read at 450 nm. Data is presented as the ratio of the expression of enhanced (containing an intron, HBVenh, or both) vector to a base vector.

Please replace the paragraph on page 77, beginning on line 6, with the following rewritten paragraph:

ELISA plates (Costar) were incubated overnight at 4.degree. C. with 100 .mu.l of goat anti-human IgG (Sigma #13382, 1/1000 dilution in carbonate coating buffer) per well. All subsequent incubations lasted 1 hour at room temperature with washes (10 mM Tris, 150 mM NaCl, 0.1% Brij-35, pH8.0) between each incubation. The wells were then blocked with 100 .mu.l of 5% dry in PBS, followed by incubation with serially diluted media supernatants in dilution buffer (2% dry milk, PBS, 0.05% TWEEN[®]-20 polysorbate surfactant). This was followed by incubation with 100 .mu.l of goat anti-human IgG/HRP (Sigma #A6029, 1/5000 dilution in dilution buffer) per well, followed by color development using 100 .mu.l of TMB microwell substrate. The reactions were stopped with 100 .mu.l of 1 M H₂SO₄, and read at 450 nm. Data is presented as the ratio of the expression of the experimental signal peptides to the human TPA signal peptide vector.

Please replace the paragraph on page 79, beginning on line 11, with the following rewritten paragraph:

At six weeks, blood samples were harvested from vaccinated animals. A volume of serum isolated from these samples was placed into wells of a reaction vessel supplied with the AUSAB.RTM. EIA Diagnostic Kit (Abbott Laboratories, Abbott Park, Ill.). The volume of sera added depended upon the antibody titer of the sample, and the sample was diluted with sample dilution buffer to fall within values obtainable with a quantification panel. 200 .mu.l from each vial of the AUSAB.RTM. Quantification Panel (Abbott Laboratories, Abbott Park, Ill.) was added to wells of the reaction vessel. To each well a bead was added, after which the vessel was sealed and incubated for two hours at 40.degree. C. The wells were then washed of all liquid reaction components. To each washed well was added 200 .mu.l of conjugate mix, after which the vessel was sealed and incubated for two hours at 40.degree. C. The wells were then washed of all liquid reaction components. The beads were transferred to new tubes after which 300 .mu.l of color development buffer was added. At 30 minutes, the color development reaction was stopped by the addition of 1 M sulfuric acid, and the absorbance of the reactions was measured at 490 nm in a Quantum **QUANTUM** II.RTM. spectrophotometer (Abbott Laboratories, Abbott Park, Ill.). This spectrophotometer calculates the antibody levels of a sample by comparing the absorbance of the sample with a standard

curve generated with the quantification panel. These antibody levels were then corrected for dilution factors. The data shown in FIG. 7 are the geometric mean titers of all animals vaccinated with a particular vector.

Please replace the paragraph on page 80, beginning on line 7, with the following rewritten paragraph:

96-well Costar medium-binding ELISA plates (Fisher Scientific, Pittsburgh, Pa.) were coated with a synthetic Flu M2 peptide (QCB/Biosource, Hopkinton, Mass.) at a concentration of 1 ug/ml in PBS (Biowhittaker, Walkerville, Md.) and incubated overnight at 4.degree. C. The plates were washed three times with 10 mM Tris (Sigma, St. Louis, Mo.)/150 mM NaCl (Fisher Scientific)/0.1% Brij-35. (Sigma), then blocked with 5% dry milk (Bio Rad Laboratories, Melville, N.Y.) in PBS for 1 hour at room temperature. All subsequent incubations were at room temperature for one hour and washes between each incubation were as stated above. Sample mouse sera, a standard (high titer, anti-M2 mouse sera) and a negative control (anti-HBsAg mouse sera) were diluted in 2% dry milk/PBS/0.05% Tween **TWEEN**[®]-20 polysorbate surfactant (Sigma) and incubated in the ELISA plates. Goat anti-mouse IgG (H+L) biotin conjugated antibody (Southern Biotechnology Associate, Birmingham, Ala.) diluted 1:8000 in 2% dry milk/PBS/0.05% Tween **TWEEN**[®]-20 polysorbate surfactant and streptavidin-horseradish peroxidase conjugate (Southern Biotechnology) diluted 1:8000 in PBS/0.1% Tween **TWEEN**[®]-20 polysorbate surfactant followed. Color was developed using TMB substrate (BioFX, Owings Mills, Md.). The reactions were stopped with 1 M H₂SO₄ and the plates read at 450 nm with an Emax precision microplate reader (Molecular Devices, Sunnyvale, Calif.). SoftMax Pro 4.1 software (Molecular Devices) was used to calculate endpoint titers using a four-parameter analysis. Titers were normalized to the standard serum, which had a pre-determined titer, to minimize assay-to-assay and plate-to-plate variation. Results are shown in FIG. 7.

Please replace the paragraph on page 81, beginning on line 2, with the following rewritten paragraph:

96-well Costar medium-binding ELISA plates (Fisher Scientific, Pittsburgh, Pa.) were coated with HSV gD (Viral Therapeutics, Ithaca, N.Y.) protein at a concentration of 1 ug/ml in PBS (Biowhittaker, Walkerville, Md.) and incubated overnight at 4.degree. C. The plates were washed three times with 10 mM Tris (Sigma, St. Louis, Mo.)/150 mM NaCl (Fisher Scientific)/0.1% Brij-35 (Sigma), then blocked with 5% dry milk (Bio Rad Laboratories, Melville, N.Y.) in PBS for 1 hour at room temperature. All subsequent incubations were at room temperature for one hour and washes between each incubation were as stated above. Sample mouse sera, a standard (high titer, anti-gD mouse sera) and a negative control (anti HBsAg mouse sera) were diluted in 2% dry milk/PBS/0.05% TWEEN -20 polysorbate surfactant (Sigma) and incubated in the ELISA plates. Goat anti-mouse IgG (H+L) biotin conjugated antibody (Southern Biotechnology Associate, Birmingham, Ala.) diluted 1:8000 in 2% dry milk/PBS/0.05% TWEEN -20 polysorbate surfactant and streptavidin-horseradish peroxidase conjugate (Southern Biotechnology) diluted 1:8000 in PBS/0.1% TWEEN -20 polysorbate surfactant followed. Color was developed using TMB substrate BioFX, Owings Mills, Md.). The reactions were stopped with 1 M H₂SO₄ and the plates read at 450 nm with an Emax precision microplate reader (Molecular Devices, Sunnyvale, Calif.). SoftMax Pro 4.1 software (Molecular Devices) was used to calculate endpoint titers using a four-parameter analysis. Titers were normalized to the standard serum, which had a pre-determined titer, to minimize assay-to-assay and plate-to-plate variation. Results are shown in FIG. 7.